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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
FOLEY,S	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/642,492	Applicant(s) VAN NEST ET AL.	
	Examiner Shanon A. Foley	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-37 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-37 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Objections

Claim 22 is objected to because of the following informalities: "antibodies is" should be "antibodies are". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and confusing because it cannot be determined what a second antigen could be without mention of a first antigen. Also, the claim states that an immune response is modulated to the second antigen upon exposure. What if the individual never encounters the second antigen? How can it be determined that exposure to the first antigen will elicit an immune response to a second antigen if the second antigen is never encountered? Is exposure to the second antigen part of a treatment, or is it a pathogen of some sort?

Claim 2 is contradictory to itself. The claim is drawn to the first antigen being administered in the absence of the second antigen, but further states that exposure to the second antigen is occurs concurrently with the first antigen. For the exposure to the second antigen to occur at the same time as administration of the first antigen, the second antigen would also have to be administered.

Claim 5 is drawn to the immunomodulatory polynucleotide and the first antigen which are associated by a platform molecule. It is unclear what is intended by a "platform molecule". Rose (J. Ther. Biol. 1998; 195: 111-128) teaches using a platform molecule to treat cancer where the platform is an insoluble material that has the ability to bind various agents, see the last paragraph on page 111 through the of the introduction on page 112 and figure 1 on page 114. Is this what is meant by platform molecule?

Claim 8 states that the first antigen is administered before exposure to the second antigen. The claim is vague because it cannot be predicted when exposure to an antigen will occur. Furthermore, in most cases in the environment, it cannot be immediately determined that an exposure has taken place.

Claims 9 and 10 are drawn to a time frame in which the individual is to be exposed to the second antigen. If the second antigen is a pathogen, how can an exposure be planned or predicted? Claim 9 also uses vague language "less than about" to describe when exposure to a second antigen might occur.

Claims 11 and 12 are drawn to the site of administration of the ISS and first antigen as being the same or different from where exposure to the second antigen occurs. Unless the second antigen is also administered, how could it be known where a pathogen made entry?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2 and 9-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for encountering a second pathogen at a specific time and

place upon administration, does not reasonably provide enablement for encountering a second pathogen at a specific time and place where it is encountered in the environment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

It cannot be discerned from the claims whether the second antigen is a part of the treatment, or if the second antigen is a pathogen that the individual is to be protected from. The specification states that the second antigen may be administered or encountered by the environment, see for example, page 6, lines 8-31. The nature of the invention is to apply an ISS in conjunction with an antigen to protect against a pathogen that may be encountered in the environment. Claims 2, 9, and 10 are drawn to a method of modulating an immune response to a second antigen by administering an immunostimunlatory polynucleotide (ISS) and a first antigen. Claims 11 and 12 are drawn to administering the first antigen complex at the same site or at a different site of exposure to the second antigen. Administration of this complex is said to happen concurrently, upon exposure, or "less than about" 10 days before exposure to the second antigen. There is no way to predict exactly where or when exposure to an antigen will occur in the environment. If there were, it would be possible to avoid them altogether. There is no guidance or working example in the specification that would enable the skilled artisan a way to predict the time and exact location of a pathogen, except when a second pathogen is administered directly. Therefore, due to the breadth of the claims, the nature of the invention, the absence of working examples directed to how one could predict exactly where and when an individual would come into contact with a pathogen, it is determined that a an undue amount of

experimentation would be required by one skilled in the art to make and/or use the invention in its full scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6-8, 13, 14, 17, 20-36 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Schwartz et al. (WO 98/55495).

The claims are drawn to a method of modulating a Th1 immune response to a second antigen by administering an immunostimulatory molecule (ISS) and a first antigen before an individual encounters the second antigen. The first antigen can be a variety of antigens, such as an allergen or a virus polypeptide, with a carrier molecule. The ISS comprises various short sequence residues in claims 24-31.

Schwartz et al. clearly anticipate claims 1-4, 6-8, 13, 14, 15, 17, 20-36. See the abstract, page 13, lines 26 through page 16, line 29; page 21, line 13 through page 24, line 6; and examples 1-5, pages 27 through page 32; also see claims 1-4, 25-36, 43-51, 56-70, and the sequence alignment of SEQ ID NO: 1 provided.

Claims 1-4, 6-8, 13, 14, 17 and 20-36 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Carson et al. (WO 98/16247).

Carson et al. clearly anticipate claims1-4, 6-8, 13, 14, and 20-36. See the abstract and claims 54-111, pages 3-6, 10-33, examples on pages 35-39, and the sequence alignment of SEQ ID NO: 1 provided.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al. or Carson et al. as applied to claims 1-4, 6-8, 13, 14, 17, 20-36 above, and further in view of Rose (J. Ther. Biol. 1998; 195: 111-128).

Claim 5 is drawn to an immunomodulatory polynucleotide and a first antigen proximately associated by a platform molecule. See the teachings of Schwartz et al. or Carson et al. above. Neither reference teaches the use of a platform molecule. However, Rose teaches using a platform molecule to treat cancer where the platform is an insoluble material that has the ability to bind various agents, see the last paragraph on page 111 through the of the introduction on page 112 and figure 1 on page 114. Since the teachings of Rose demonstrate that various components may be proximately associated by a platform molecule, the limitation of a platform molecule in claim 5 would have been an obvious modification to the other mechanisms of proximity taught by Schwartz et al. or Carson et al.

Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al. or Carson et al. and Rose as applied to claims 1-8, 13, 14, 17, 20-36 above, and further in view of Lee et al. (Ann Med. 1998; 30: 460-468).

The claim is drawn to the viral polypeptide, where the polypeptide is influenza nucleocapsid protein. See the teachings of Schwartz et al. or Carson et al. and Rose above. None of the references teach influenza nucleocapsid protein. However, Lee et al. teach that this protein is the least effected by antibody-induced antigenic drift and studies using DNA encoding this protein have demonstrated protection, see "infectious diseases" on page 465. One of ordinary skill in the art would have been motivated to incorporate a protein into a treatment composition that has already demonstrated protective properties in other studies. Furthermore, one of ordinary skill in the art would have had a reasonable expectation in producing the claimed invention because Schwartz et al. or Carson et al. teach compositions and methods comprising ISS and proteins that modulate the immune response and Lee et al. also teach subsequent Th1 responses upon administration of ISS with DNA encoded antigens, see "mechanism of action..." on pages 463-464. Therefore, the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Claims 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al. or Carson et al., and Rose, as applied to claims 1-8, 13, 14, 17, 20-36 above, and further in view of Durali et al. (J of Virol. 1998; 72(5): 3547-3553).

The claim is drawn to the viral polypeptide, where the polypeptide is HIV gag. See the teachings of Schwartz et al. or Carson et al., Rose, and Lee et al. above. None of the references teach influenza nucleocapsid protein or HIV gag in their compositions. However, Durali et al.

teach that the gag protein is capable of cross-reactivity in different patients infected with different clades of HIV, see the abstract. Since high variability in HIV is a major obstacle in selecting an antigen for a vaccine candidate and Durali et al. have been able to identify a conserved protein, one of ordinary skill in the art would be motivated to incorporate this protein into a treatment composition. Furthermore, the skilled artisan would have a reasonable expectation in producing the claimed invention because both Schwartz et al. and Carson et al. teach that the protein portion of the composition and method could be a wide variety of proteins from viruses, see previously cited excerpts.

Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al. or Carson et al., Rose, Lee et al., and Durali et al. as applied to claims 1-8, 13-17, 20-36 above, and further in view of Anderson (US Patent 4,673,574).

The claims are drawn to using diphtheria toxin mutant CRM 197 or diphtheria toxoid as a carrier molecule. See the teachings of Carson et al., Rose, Lee et al., and Durali et al. above. None of the references teach using either diphtheria molecule. However, Anderson teaches that diphtheria toxoid or diphtheria toxin mutant CRM 197 can be use as carriers in a vaccine preparations, see column 4, lines 35-68 and example 8 in column 14, line 9 through column 16, line 44. One of ordinary skill in the art at the time the invention was made would have been motivated to use the diphtheria components taught by Anderson in the method and composition taught by taught by Schwartz et al. or Carson et al. when administering the composition to children or immunocomprised individuals because the diphtheria toxins aid in eliciting a protective immune response, have no toxicity, and can be administered safely to children, see column 5, lines 10-19 and column 14, table 7. One of ordinary skill in the art at the time the

invention was made would have had a reasonable expectation in producing the claimed invention because Schwartz et al. or Carson et al. teach that the ISS/antigen composition can be combined with any known vaccine component and the diphtheria toxins taught by Anderson are well known.

Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al. or Carson et al., Rose, Lee et al., Durali et al., and Anderson as applied to claims 1-8 and 13-36 above.

The claim is drawn to the first antigen composed of a conserved polypeptide and the second antigen administered is a variable polypeptide. See the teachings of Schwartz et al. or Carson et al., Rose, Lee et al., Durali et al., and Anderson above. Although none of the references specifically teach administering a conservative and a variable polypeptide, one of ordinary skill in the art at the time the invention was made would have been motivated to use this combination to cover a broader scope of variants in pathogens that may be encountered in the environment. From the teachings of the references, it is determined that the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon A. Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on 7:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Laurie Scheiner and James Housel can be reached at (703) 308-1122 and (703) 308-

4027, respectively. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley/SAF
July 27, 2001

LAURIE SCHEINER
PRIMARY EXAMINER